



PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference RJW/CP6219786	FOR FURTHER ACTION See Form PCT/PEA/416	
International application No. PCT/GB2004/003184	International filing date (day/month/year) 23.07.2004	Priority date (day/month/year) 24.07.2003
International Patent Classification (IPC) or national classification and IPC C07D239/48, C07D417/12, C07D401/12, C07D239/46, C07D233/88, C07D409/04, C07D263/48, C07D413/10, C07D249/14, A61K31/505, A61K31/506, A61K31/4168, A61K31/4178, A61K31/421, A61K31/4439, A61K31/496, A61P1/00		
Applicant PHARMAGENE LABORATORIES LIMITED et al		
<p>1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 7 sheets, including this cover sheet.</p> <p>3. This report is also accompanied by ANNEXES, comprising:</p> <p>a. <input checked="" type="checkbox"/> sent to the applicant and to the International Bureau) a total of 22 sheets, as follows:</p> <p><input checked="" type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).</p> <p><input type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.</p> <p>b. <input type="checkbox"/> (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).</p>		
<p>4. This report contains indications relating to the following items:</p> <p><input checked="" type="checkbox"/> Box No. I Basis of the opinion</p> <p><input type="checkbox"/> Box No. II Priority</p> <p><input checked="" type="checkbox"/> Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</p> <p><input type="checkbox"/> Box No. IV Lack of unity of invention</p> <p><input checked="" type="checkbox"/> Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p><input checked="" type="checkbox"/> Box No. VI Certain documents cited</p> <p><input type="checkbox"/> Box No. VII Certain defects in the international application</p> <p><input type="checkbox"/> Box No. VIII Certain observations on the international application</p>		
Date of submission of the demand 11.05.2005	Date of completion of this report 05.12.2005	
Name and mailing address of the international preliminary examining authority:  European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Tx: 31 651 epo nl Fax: +31 70 340 - 3016	Authorized Officer Allard, M Telephone No. +31 70 340-2002 	

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Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.
- ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
- ☐ international search (under Rules 12.3 and 23.1(b))
 - ☐ publication of the international application (under Rule 12.4)
 - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)
2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

Description, Pages

1-149 as originally filed

Claims, Numbers

1-91 received on 11.05.2005 with letter of 09.05.2005

- ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing
3. ☐ The amendments have resulted in the cancellation of:
- ☐ the description, pages
 - ☐ the claims, Nos.
 - ☐ the drawings, sheets/figs
 - ☐ the sequence listing (*specify*):
 - ☐ any table(s) related to sequence listing (*specify*):
4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
- ☐ the description, pages
 - ☐ the claims, Nos.
 - ☐ the drawings, sheets/figs
 - ☐ the sequence listing (*specify*):
 - ☐ any table(s) related to sequence listing (*specify*):

* If item 4 applies, some or all of these sheets may be marked "superseded."

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Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 1-30 (all in part)

because:

☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (specify):

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the said claims Nos. 1-30 (all in part)

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form ☐ has not been furnished

☐ does not comply with the standard

the computer readable form ☐ has not been furnished

☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

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Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	3,5,6,8,9,18,19,29-91
	No: Claims	1,2,4,7,10-17,20-28
Inventive step (IS)	Yes: Claims	3,5,6,8,9,18,19,29-91
	No: Claims	1,2,4,7,10-17,20-28
Industrial applicability (IA)	Yes: Claims	1-91
	No: Claims	-

2. Citations and explanations (Rule 70.7):

see separate sheet

Box No. VI Certain documents cited

1. Certain published documents (Rule 70.10)

and / or

2. Non-written disclosures (Rule 70.9)

see separate sheet

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Reference is made to the following documents:

- D03: US-A-2 585 910 (BARTON N ET AL) 19 February 1952 (1952-02-19)
D04: US-A-2 643 253 (SWINDEN F H ET AL) 23 June 1953 (1953-06-23)
D06: BANKS C K: "Arylaminoheterocycles. II. Arylaminoimidines" JOURNAL OF THE AMERICAN CHEMICAL SOCIETY, vol. 66, no. 7, July 1944 (1944-07), page 1131, XP002298658
D11: WO 02/092576 A (BOEHRINGER INGELHEIM PHARMACEUTICALS, INC.) 21 November 2002 (2002-11-21)
D12: WO 97/44326 A (F. HOFFMANN-LA ROCHE AG) 27 November 1997 (1997-11-27)

Remark

The validity of certain newly introduced disclaimers, which have no basis in the application as originally filed, might be questioned in a further national or regional phase, depending on the case law of the concerned Contracting State.

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The initial phase of the search revealed a very large number of documents relevant to the issue of novelty of claims 1-30. So many documents were retrieved that it is impossible to determine which parts of said claims may be said to define subject-matter for which protection might legitimately be sought (Article 6 PCT). For these reasons, a meaningful complete search over the whole breadth of said claims was impossible.

Consequently, a complete international preliminary examination of the present application is limited to those parts of the claims for which a complete international search report was established (Rule 66.1(e) PCT), *i.e.* to claims 31-91. It should in particular be understood that any positive statement as to novelty and/or inventive step exclusively relates to said

limited subject-matter.

Re Item V

**Reasoned statement with regard to novelty, inventive step or industrial applicability;
citations and explanations supporting such statement**

Novelty (Article 33(2) PCT)

The subject-matter of claims 1, 2, 4, 7, 10-17 and 20-28 lacks novelty in the light of the disclosure of D03 (also disclosing quinaldine derivatives useful as trypanocidal agents), D04 (disclosing quinazoline derivatives useful as trypanocidal agents), D06 (disclosing a naphthylamino derivative, see compound 18) and D11 (disclosing compounds useful against inflammatory bowel disease, see page 6, lines 17/18, and page 25, first two compounds). In this context it should be noted that a second medical use claim, as claim 1 and its dependent claims, cannot be rendered novel by specifying the biological mechanism of the therapeutical treatment; as D11 clearly disclose diseases falling within the ambit of 5-HT_{2B} receptor antagonists alleviation, the subject-matter of claims 1, 2, 4, 7 and 10, amongst others, lacks novelty.

The subject-matter of claims 3, 5, 6, 8, 9, 18, 19 and 29-91 is not disclosed in the available prior art, and is therefore novel.

Inventive step (Article 33(3) PCT)

The subject-matter of claims 1, 2, 4, 7, 10-17 and 20-28 lacking novelty does not offer a basis for acknowledging an inventive step.

An inventive step can be acknowledged for the subject-matter of claims 3, 5, 6, 8, 9, 18, 19 and 29-91:

D12, which is considered to represent the closest prior art, describes amongst others 4-aryl-pyrimidin-2-amines useful as 5-HT_{2B} antagonists.

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in the light of the disclosure of D12 the problem underlying and solved by the present application can be seen in the provision of further 5-HT_{2B} antagonists.

This problem is solved by the compounds of claims 3, 5, 6, 8, 9, 18, 19 and 29-91 of the present application in a manner which is neither obvious nor suggested by the teachings of the available prior art.

Industrial applicability (Article 33(4) PCT)

The methods, compositions and compounds of claims 1-91 can be used in the pharmaceutical industry.